

# Optimizing Narrowband UVB Phototherapy: Is It More Challenging for Your Older Patients?

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## PRACTICE POINTS

- Narrowband UVB (NB-UVB) phototherapy remains a safe and efficacious nonpharmacologic treatment for dermatologic conditions in older and younger adults.
- Compared to younger adults, older adults using the same protocols need similar or even fewer treatments to achieve high levels of clearance.
- Individuals taking 3 or more photosensitizing medications, regardless of age, may be at higher risk for substantial erythema with NB-UVB phototherapy.
- Phototherapy program monitoring is important to ensure quality care and investigate opportunities for care optimization.

Narrowband UVB (NB-UVB) phototherapy remains versatile, safe, and efficacious for multiple dermatologic conditions even with recent pharmacologic treatment advances. Polypharmacy contributes to prescribers pursuing phototherapy as a nonpharmacologic treatment, but some wonder if it is as effective and safe for older patients. This study aimed to determine if NB-UVB is equally effective in both older and younger adults treated with the same protocol and to examine the association between photosensitizing medications, clearance, and erythema rates in older vs younger adults.

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Even with recent pharmacologic treatment advances, narrowband UVB (NB-UVB) phototherapy remains a versatile, safe, and efficacious adjunctive or

exclusive treatment for multiple dermatologic conditions, including psoriasis and atopic dermatitis.<sup>1-9</sup> Some providers choose NB-UVB phototherapy as a first-line treatment for older adult patients who frequently use multiple treatment modalities for more than 1 health condition. Older adults with atopic dermatitis and psoriasis are at higher risk for comorbidities such as autoimmune disorders, diabetes mellitus, dyslipidemia, sleep disorders, neuropsychiatric disorders, and cardiovascular disease that can complicate treatment compared with their peers without these dermatologic diagnoses.<sup>10-12</sup> Polypharmacy (ie, the use of 5 or more daily medications), frequently associated with these conditions, contributes to prescribers pursuing NB-UVB phototherapy as a nonpharmacologic treatment, but some providers wonder if it is as effective and safe for their older patients compared with younger patients.

In a prior study, Matthews et al<sup>13</sup> reported that 96% (50/52) of patients older than 65 years achieved medium to high levels of clearance with NB-UVB phototherapy. Nonetheless, 2 other findings in this study related to the number of treatments required to achieve clearance (ie, clearance rates) and erythema rates prompted further investigation. The first finding was higher-than-expected clearance rates. Older adults had a clearance rate with a mean of 33 treatments compared to prior studies featuring mean clearance rates of 20 to 28 treatments.<sup>7,8,14-16</sup> This finding resembled a study in the United Kingdom<sup>17</sup> with a median clearance rate in older adults of 30 treatments. In contrast, the median clearance rate from a study in Turkey<sup>18</sup> was 42 treatments in older adults. We hypothesized that more photosensitizing medications used in

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older vs younger adults prompted more dose adjustments with NB-UVB phototherapy to avoid burning (ie, erythema) at baseline and throughout the treatment course. These dose adjustments may have increased the overall clearance rates. If true, we predicted that younger adults treated with the same protocol would have cleared more quickly, either because of age-related differences or because they likely had fewer comorbidities and therefore fewer medications.

The second finding from Matthews et al<sup>13</sup> that warranted further investigation was a higher erythema rate compared to the older adult study from the United Kingdom.<sup>17</sup> We hypothesized that potentially greater use of photosensitizing medications in the United States could explain the higher erythema rates. Although medication-induced photosensitivity is less likely with NB-UVB phototherapy than with UVA, certain medications can cause UVB photosensitivity, including thiazides, quinidine, calcium channel antagonists, phenothiazines, and non-steroidal anti-inflammatory drugs.<sup>8,19,20</sup> Therefore, photosensitizing medication use either at baseline or during a course of NB-UVB phototherapy could increase the risk for erythema. Age-related skin changes also have been considered as a potential cause for erythema. One study found that the skin of older patients was more sensitive than younger patients, resulting in a lower minimal erythema dose (MED)<sup>14</sup>—the lowest UV dose that results in

erythema.<sup>21</sup> Others, however, found similar MEDs across age groups, but older adults experienced more intense erythema in the late phase of NB-UVB treatment.<sup>22,23</sup> Such conflicting findings indicate that questions remain regarding the risk for erythema in older patients and if photosensitizing medications are responsible for an increased risk.

This retrospective study aimed to determine if NB-UVB phototherapy is equally effective in both older and younger adults treated with the same protocol; to examine the association between the use of photosensitizing medications and clearance rates in both older and younger adults; and to examine the association between the use of photosensitizing medications and erythema rates in older vs younger adults.

## Methods

**Study Design and Patients**—This retrospective cohort study used billing records to identify patients who received NB-UVB phototherapy at 3 different clinical sites within a large US health care system in Washington (Group Health Cooperative, now Kaiser Permanente Washington), serving more than 600,000 patients between January 1, 2012, and December 31, 2016. The institutional review board of Kaiser Permanente Washington Health Research Institute approved this study (IRB 1498087-4). Younger adults were classified as those 64 years or younger and older adults as

**TABLE 1. Patient Demographics**

Characteristic	Total patients (N=172)	Younger adults aged ≤64 y (N=102)	Older adults aged ≥65 y (N=70)
Sex, n (%)			
Male	86 (50)	48 (47.1)	38 (54.3)
Female	86 (50)	54 (52.9)	32 (45.7)
Mean age (SD), y	57.4 (16.1)	47.0 (12.0)	72.4 (6.7)
Age range, y	23–91	23–64	65–91
Fitzpatrick skin type, n (%)			
I	14 (8.1)	6 (5.9)	8 (11.4)
II	68 (39.5)	45 (44.1)	23 (32.9)
III	64 (37.2)	34 (33.3)	30 (42.9)
IV	24 (14)	16 (15.7)	8 (11.4)
V	2 (1.2)	1 (1.0)	1 (1.4)
VI	0 (0)	0 (0)	0 (0)
Prior phototherapy treatment, n (%)	68 (39.5)	41 (40.2)	27 (38.6)

those 65 years and older at the start of their phototherapy regimen. A power analysis determined that the optimal sample size for this study was 250 patients.

Individuals were excluded if they had fewer than 6 phototherapy treatments; a diagnosis of vitiligo, photosensitivity dermatitis, morphea, or pityriasis rubra pilaris; and/or treatment of the hands or feet only.

**Phototherapy Protocol**—Using a 48-lamp NB-UVB unit, trained phototherapy nurses provided all treatments following standardized treatment protocols<sup>13</sup> based on previously published phototherapy guidelines.<sup>24</sup> Nurses determined each patient's disease clearance level using a 3-point clearance scale (high, medium, low).<sup>13</sup> Each patient's starting dose was determined based on the estimated MED for their skin phototype. If the patient was using photosensitizing medications, the protocol indicated a need for a decreased starting dose—down 25% to 50%—depending on the presumed level of photosensitivity. All clinical sites used the same protocol, but decisions about adjustments within this range were made by individual registered nurses and dermatologists, which could lead to variability across sites. Protocols also directed nurses to query patients about specific treatment responses, including erythema, tenderness, or itching; how their condition was responding; use of photosensitizing medications; missed treatments; and placement of shielding. Doses were adjusted accordingly.

**Statistical Analysis**—Data were analyzed using Stata statistical software (StataCorp LLC). Univariate analyses were used to examine the data and identify outliers, bad values, and missing data, as well as to calculate descriptive statistics. Pearson  $\chi^2$  and Fisher exact statistics were used to calculate differences in categorical variables. Linear multivariate regression models and logistic multivariate models were

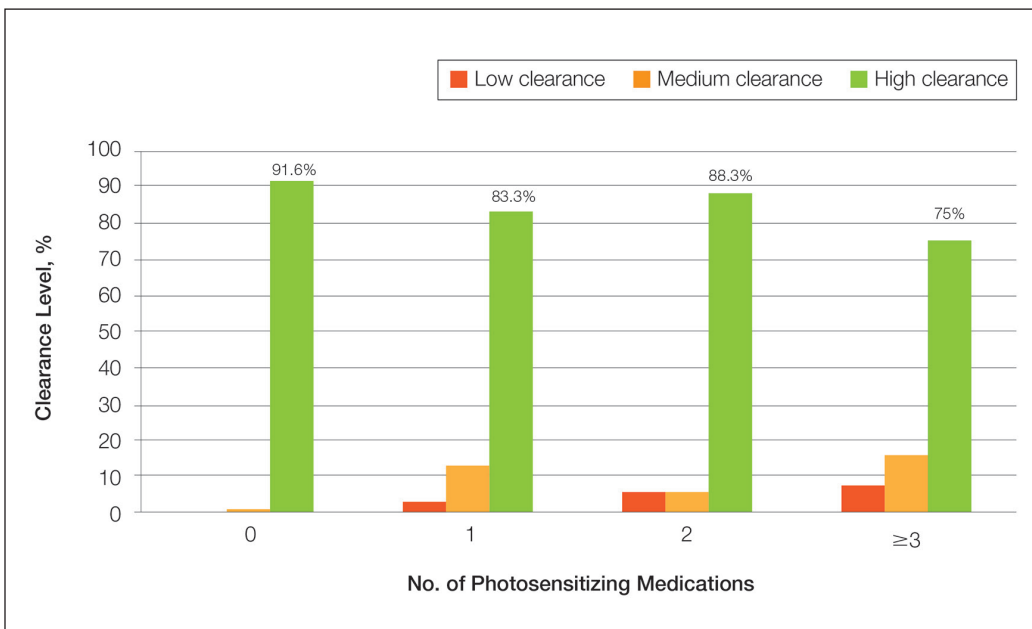
used to examine statistical relationships between variables. Statistical significance was defined as  $P \leq .05$ .

## Results

**Patient Characteristics**—Medical records were reviewed for 172 patients who received phototherapy between 2012 and 2016. Patients ranged in age from 23 to 91 years, with 102 patients 64 years and younger and 70 patients 65 years and older. Tables 1 and 2 outline the patient characteristics and conditions treated.

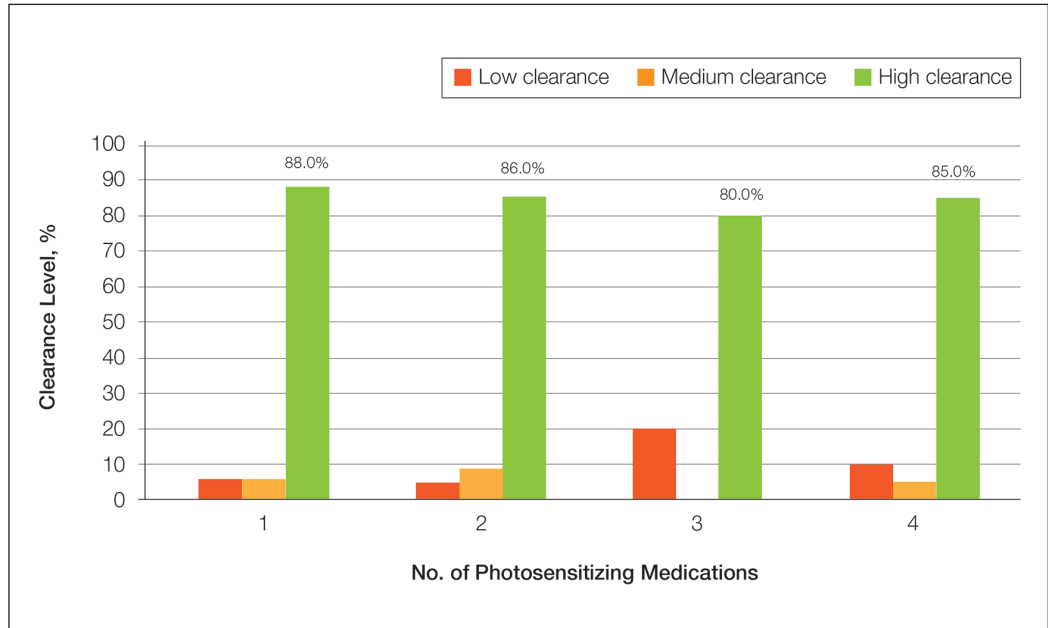
**Phototherapy Effectiveness**—Narrowband UVB phototherapy was found to be equally effective in older vs younger adults, with 82.9% of older adults ( $n=58$ ) achieving a high level of clearance vs 80.4% ( $n=82$ ) of younger adults, and 5.7% ( $n=4$ ) of older adults achieved a medium level of clearance vs 10% ( $n=10$ ) of younger adults (Table 3). Although older adults had slightly faster clearance rates on average (34.6 vs 37.2 treatments), these differences were not significant.

**Photosensitizing Medications, Clearance Levels, and Clearance Rates**—There was no significant association between clearance levels and number of photosensitizing medications in either younger (Figure 1) or older (Figure 2) adults. There was a wide range of clearance rates in both groups (Table 3), but no relationship was identified between clearance rates and photosensitizing medications or age (Figure 3). Clinic C had higher overall clearance rates for both age groups compared to the other clinics (Figure 4), but the clearance levels were still equivalent. No consistent pattern emerged indicating that age was a factor for the slower clearance at this site, and no relationship was identified between taking photosensitizing medications and clearance levels (Fisher exact test,  $P=.467$ ) or clearance rates ( $t[149]=0.75$ ;  $P=.45$ ).

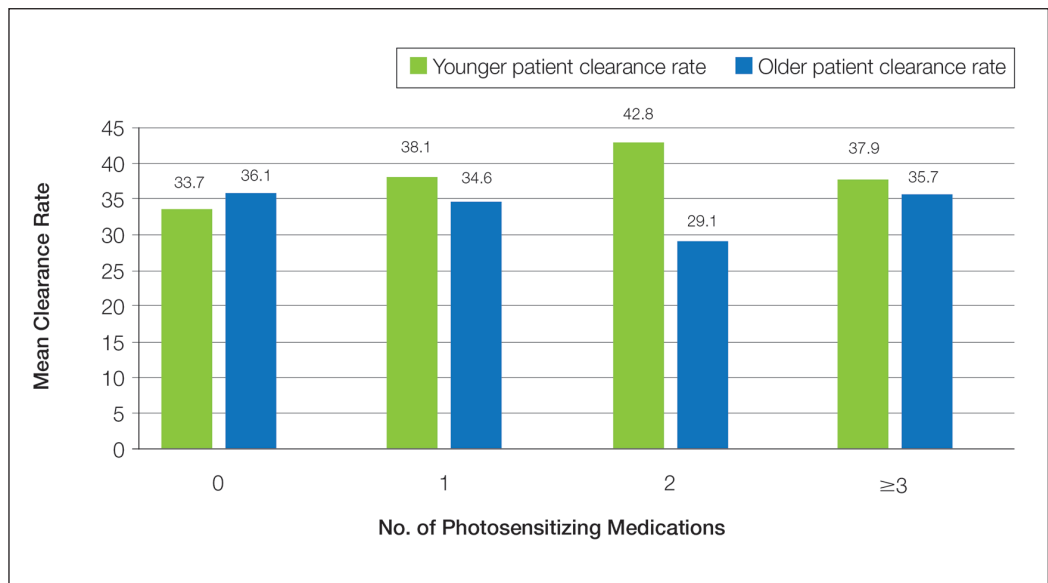


**FIGURE 1.** Clearance levels and photosensitizing medications in younger adults.

**FIGURE 2.** Clearance levels and photosensitizing medications in older adults.



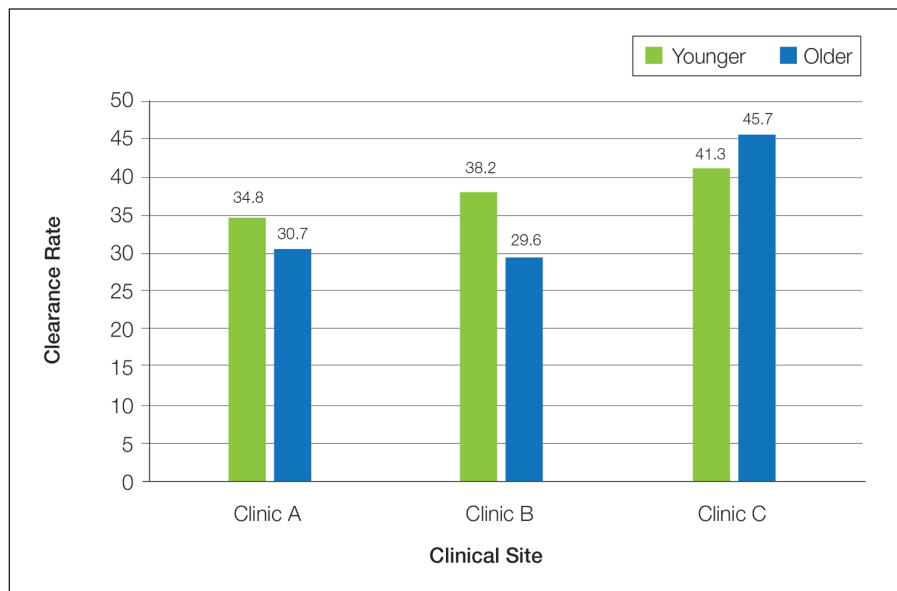
**FIGURE 3.** Number of photosensitizing medications and mean clearance rate.



*Frequency of Treatments and Clearance Rates*—Older adults more consistently completed the recommended frequency of treatments—3 times weekly—compared to younger adults (74.3% vs 58.5%). However, all patients who completed 3 treatments per week required a similar number of treatments to clear (older adults, mean [SD]: 35.7 [21.6]; younger adults, mean [SD]: 34.7 [19.0];  $P=.85$ ). Among patients completing 2 or fewer treatments per week, older adults required a mean (SD) of only 31 (9.0) treatments to clear vs 41.5 (21.3) treatments to clear for younger adults, but the difference was not statistically significant ( $P=.08$ ). However, even those with suboptimal frequency ultimately achieved similar clearance levels.

*Photosensitizing Medications and Erythema Rates*—Many patients in both age groups took medications that

listed photosensitivity as a potential side effect (77.1% of older adults and 60.8% of younger adults). Of them, most patients took only 1 or 2 photosensitizing medications. However, significantly more older patients took 3 or more photosensitizing medications (28.6% vs 12.7%;  $P=.01$ ) (Table 3). Asymptomatic (grade 1) erythema was unrelated to medication use and quite common in all adults (48.6% of older adults and 60.8% of younger adults). Most patients had only a few episodes of grade 1 erythema (mean [SD], 1.2 [2.9] in older adults and 1.6 [2.2] in younger adults). More older adults had grade 2 erythema (28.6%) compared to younger adults (17.6%). Patients using 3 or more photosensitizing medications were twice as likely to experience grade 2 erythema. Grades 3 and 4 erythema were extremely rare; none of



**FIGURE 4.** Clearance rates by site and age.

the patients stopped phototherapy because they experienced erythema.

Overall, phototherapy nurses adjusted the starting dose according to the phototype-based protocol an average of 69% of the time for patients on medications with photosensitivity listed as a potential side effect. However, the frequency depended significantly on the clinic (clinic A, 24%; clinic B, 92%; clinic C, 87%) ( $P \leq .001$ ). Nurses across all clinics consistently decreased the treatment dose when patients reported starting new photosensitizing medications. Patients with adjusted starting doses had slightly but not significantly higher clearance rates compared to those without (mean, 37.8 vs 35.5;  $t(104) = 0.58$ ;  $P = .56$ ).

## Comment

**Comparisons to Prior Studies**—This study confirmed that phototherapy is equally effective for older and younger adults, with approximately 90% reaching medium to high clearance levels with approximately 35 treatments in both groups. Prior studies of all age groups found that patients typically cleared with an average of 20 to 28 treatments.<sup>7,8,14-16</sup> In contrast, the findings in older adults from this study were similar to the older adult study from the United Kingdom that reported a 91% clear/near clear rate with an average of 30 treatments.<sup>17</sup> The clearance level also was similar to the older adult study in Turkey<sup>18</sup> that reported 73.7% (70/95) of patients with psoriasis achieved a minimum psoriasis area severity index of 75, indicating 75% improvement from baseline.

**Impact of Photosensitizing Medications on Clearance**—Photosensitizing medications and treatment frequency were 2 factors that might explain the slower clearance rates in younger adults. In this study, both groups of patients used similar numbers of photosensitizing medications, but more older adults were taking 3 or more

medications (Table 3). We found no statistically significant relationship between taking photosensitizing medications and either the clearance rates or the level of clearance achieved in either age group.

**Impact of Treatment Frequency**—Weekly treatment frequency also was examined. One prior study demonstrated that treatments 3 times weekly led to a faster clearance time and higher clearance levels compared with twice-weekly treatment.<sup>7</sup> When patients completed treatments twice weekly, it took an average of 1.5 times more days to clear, which impacted cost and clinical resource availability. The patients ranged in age from 17 to 80 years, but outcomes in older patients were not described separately.<sup>7</sup> Interestingly, our study seemed to find a difference between age groups when the impact of treatment frequency was examined. Older adults completed nearly 4 fewer mean treatments to clear when treating less often, with more than 80% achieving high levels of clearance, whereas the younger adults required almost 7 more treatments to clear when they came in less frequently, with approximately 80% achieving a high level of clearance. As a result, our study found that in both age groups, slowing the treatment frequency extended the treatment time to clearance—more for the younger adults than the older adults—but did not significantly change the percentage of individuals reaching full clearance in either group.

**Erythema Rates**—There was no association between photosensitizing medications and erythema rates except when patients were taking at least 3 medications. Most medications that listed photosensitivity as a possible side effect did not specify their relevant range of UV radiation; therefore, all such medications were examined during this analysis. Prior research has shown UVB range photosensitizing medications include thiazides, quinidine, calcium channel antagonists, phenothiazines, and nonsteroidal anti-inflammatory drugs.<sup>19</sup> A sensitivity analysis that

focused only on these medications found no association between them and any particular grade of erythema. However, patients taking 3 or more of any medications listing photosensitivity as a side effect had an increased risk for grade 2 erythema.

Erythema rates in this study were consistent with a 2013 systematic review that reported 57% of patients with asymptomatic grade 1 erythema.<sup>25</sup> In the 2 other comparative older adult studies, erythema rates varied widely: 35% in a study from Turkey<sup>18</sup> compared to only 1.89% in a study from the United Kingdom.<sup>17</sup>

The starting dose for NB-UVB may drive erythema rates. The current study's protocols were based on an estimated MED that is subjectively determined by the dermatology provider's assessment of the patient's skin

sensitivity via examination and questions to the patient about their response to environmental sun exposure (ie, burning and tanning)<sup>26</sup> and is frequently used to determine the starting dose and subsequent dose escalation. Certain medications have been found to increase photosensitivity and erythema,<sup>20</sup> which can change an individual's MED. If photosensitizing medications are started prior to or during a course of NB-UVB without a pretreatment MED, they might increase the risk for erythema. This study did not identify specific erythema-inducing medications but did find that taking 3 or more photosensitizing medications was associated with increased episodes of grade 2 erythema. Similarly, Harrop et al<sup>8</sup> found that patients who were taking photosensitizing medications were more likely to have grade 2

**TABLE 2. Conditions Treated and Comorbidities**

Characteristic	Total patients, n (%) (N=172)	Younger adults aged ≤64 y, n (%) (N=102)	Older adults aged ≥65 y, n (%) (N=70)
Conditions treated <sup>a</sup>			
Psoriasis	112 (65.1)	77 (75.5)	35 (50.0)
Dermatitis	44 (25.6)	22 (21.6)	22 (31.4)
Mycosis fungoides	6 (3.5)	0 (0)	6 (8.6)
Pruritus	6 (3.5)	1 (1.0)	5 (7.1)
Prurigo nodularis	2 (1.2)	0 (0)	2 (2.9)
Rash, nonspecific	1 (0.6)	0 (0)	1 (1.4)
Other	5 (2.9)	3 (2.9)	2 (2.9)
Relevant comorbidities			
Tobacco use	19 (11.0)	14 (13.7)	5 (7.1)
Alcohol overuse/abuse	15 (8.7)	10 (9.8)	5 (7.1)
Psoriatic arthritis	19 (11.0)	15 (14.7)	4 (5.7)
Hypertension	86 (50)	35 (34.3)	51 (72.9)
Myocardial infarction	8 (4.7)	2 (2.0)	6 (8.6)
Hyperlipidemia	72 (41.9)	32 (31.4)	40 (57.1)
Obstructive sleep apnea	35 (20.3)	17 (16.7)	18 (25.7)
Diabetes	33 (19.2)	19 (18.6)	14 (20.0)
Depression	38 (22.1)	25 (24.5)	13 (18.6)
Obesity (BMI >30)	61 (35.5)	39 (38.2)	22 (31.4)

Abbreviation: BMI, body mass index.

<sup>a</sup>Patients could be assigned to more than 1 treatment group.

or higher erythema, despite baseline MED testing, which is an established safety mechanism to reduce the risk and severity of erythema.<sup>14,20,27</sup> The authors of a recent study of older adults in Taiwan specifically recommended MED testing due to the unpredictable influence of polypharmacy on MED calculations in this population.<sup>28</sup> Therefore, this study's use of an estimated MED in older adults may have influenced the starting dose as well as the incidence and severity of erythemic events. Age-related skin changes likely are ruled out as a consideration for mild erythema by the similarity of grade 1 erythema rates in

both older and younger adults. Other studies have identified differences between the age groups, where older patients experienced more intense erythema in the late phase of UVB treatments.<sup>22,23</sup> This phenomenon could increase the risk for a grade 2 erythema, which may correspond with this study's findings.

Other potential causes of erythema were ruled out during our study, including erythema related to missed treatments and shielding mishaps. Other factors, however, may impact the level of sensitivity each patient has to phototherapy, including genetics, epigenetics, and

**TABLE 3. Summary of Photosensitizing Medication Utilization, Clearance Rates, Clearance Levels, and Erythema Rates**

Characteristic	Total patients (N=172)	Younger adults aged ≤64 y (N=102)	Older adults aged ≥65 y (N=70)
Photosensitizing medication use, n (%)			
None	56 (32.6)	40 (39.2)	16 (22.8)
1	53 (30.8)	30 (29.4)	23 (32.9)
2	30 (17.4)	19 (18.6)	11 (15.7)
≥3	33 (19.2)	13 (12.7)	20 (28.6)
Treatments to achieve medium to high clearance			
Range	11–145	11–126	16–145
Mean (SD)	36.1 (19.8)	37.2 (20.1)	34.6 (19.4)
Median	31	31	29.5
IQR	24–41	25–42	24–38
Clearance level, n (%)			
High	140 (81.4)	82 (80.4)	58 (82.9)
Medium	14 (8.1)	10 (10)	4 (5.7)
Low	9 (5.2)	3 (2.9)	6 (8.6)
Ongoing treatments	9 (5.2)	7 (6.9)	2 (2.9)
Erythema, n (%) <sup>a</sup>			
None	65 (37.8)	36 (35.3)	29 (41.4)
Grade 1	96 (55.8)	62 (60.8)	34 (48.6)
Grade 2	38 (22.1)	18 (17.6)	20 (28.6)
Grade 3	3 (1.7)	3 (2.9)	0 (0)
Grade 4	1 (0.6)	0 (0)	1 (1.4)

Abbreviation: IQR, interquartile range.

<sup>a</sup>Some patients experienced more than 1 grade of erythema.

cumulative sun damage. With NB-UVB, near-erythemogenic doses are optimal to achieve effective treatments but require a delicate balance to achieve, which may be more problematic for older adults, especially those taking several medications.

**Study Limitations**—Our study design made it difficult to draw conclusions about rarer dermatologic conditions. Some patients received treatments over years that were not included in the study period. Finally, power calculations suggested that our actual sample size was too small, with approximately one-third of the required sample missing.

**Practical Implications**—The goals of phototherapy are to achieve a high level of disease clearance with the fewest number of treatments possible and minimal side effects. Skin phototype-driven standardized doses based on estimated MED may be conservatively low to minimize the risk of side effects (eg, erythema), which could slow the treatment progression. Thus, basing the starting dose on individual MED assessments may improve clearance rates. This study also confirmed that phototherapy is safe with minimal erythema in adults of all ages. The erythema episodes that patients experienced were few and mild, but because of greater rates of grade 2 erythema in patients on 3 or more photosensitizing medications, consideration of MED testing in both age groups might optimize doses at baseline and prompt caution for subsequent dose titration in this subset of patients.

The extra staff training and patient monitoring required for MED testing likely is to add value and preserve resources if faster clearance rates could be achieved and may warrant further investigation. Phototherapy centers require standardized treatment protocols, diligent well-trained staff, and program monitoring to ensure consistent care to all patients. This study highlighted the ongoing opportunity for health care organizations to conduct evidence-based practice inquiries to continually optimize care for their patients.

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